

WHAT IS CLAIMED IS:

1. A C-terminal amidated human parathyroid hormone analog PTH 1-32-NH₂ (C-terminal amidated SEQ ID No: 20).

2. A C-terminal amidated human parathyroid hormone analog PTH 1-33-NH₂ (C-terminal amidated SEQ ID No: 21).

3. A pharmaceutical composition comprising a pharmaceutically effective amount of a C-terminal amidated human parathyroid hormone analog selected from the group of a C-terminal amidated SEQ ID No 20 and a C-terminal amidated SEQ ID No 21, and a pharmaceutically acceptable carrier.

4. The pharmaceutical composition of claim 3, wherein said a C-terminal amidated human parathyroid hormone analog is C-terminal amidated SEQ ID No 20.

5. The pharmaceutical composition of claim 3, wherein said a C-terminal amidated human parathyroid hormone analog is C-terminal amidated SEQ ID No 21.

6. The pharmaceutical composition of claim 3, wherein said composition is suitable for oral delivery.

7. The pharmaceutical composition of claim 6 further comprising at least one agent selected from the group of a pharmaceutically acceptable pH-lowering agent, a protease inhibitor, and a combination thereof.

8. The pharmaceutical composition of claim 7 further comprising an acid resistant protective vehicle effective to transport said pharmaceutical composition

through the stomach of a patient while preventing contact between said active peptide agent and stomach proteases.

9. The pharmaceutical composition of claim 7, wherein said pH-lowering agent is present in said pharmaceutical composition in a quantity which, if said composition were added to ten milliliters of 0.1M aqueous sodium bicarbonate solution, would be sufficient to lower the pH of said solution to no higher than 5.5.

10. The pharmaceutical composition of claim 7, wherein said pH-lowering agent is present in a quantity which, if said composition were added to ten milliliters of 0.1M aqueous sodium bicarbonate solution, would be sufficient to lower the pH of said solution to no higher than 3.5.

11. The pharmaceutical composition of claim 7, wherein said protease inhibitor is a stomach and/or intestine protease inhibitor.

12. The pharmaceutical composition of claim 7, wherein said protease inhibitor inhibits an enzyme selected from the group consisting of pepsin, trypsin, chymotrypsin, elastase, kallikrein and carboxypeptidase.

13. The pharmaceutical composition of claim 3, wherein said C-terminal amidated human parathyroid hormone analog is linked to a membrane translocator which is capable of being at least partially cleaved in vivo by an enzyme.

14. The pharmaceutical composition of claim 8, wherein said protective vehicle is present at a weight which is no more than 30% of the weight of the remainder of said pharmaceutical composition.

15. The pharmaceutical composition of claim 8, wherein said protective vehicle is present at a weight which is no more than 20% of the weight of the remainder of said pharmaceutical composition.

16. The pharmaceutical composition of claim 8, wherein said protective vehicle is present at a weight which is between 10% and 20% of the weight of the remainder of said pharmaceutical composition.

17. The pharmaceutical composition of claim 8, wherein said protective vehicle is sufficient to prevent breakdown of said pharmaceutical composition in 0.1N HCl for at least two hours, yet permits complete release of all contents of said pharmaceutical composition within 45 minutes after pH is increased to 6.3 in a dissolution bath in which said composition is rotating at 100 revolutions per minute.

18. The pharmaceutical composition of claim 8 further containing at least one absorption enhancer effective to promote bioavailability of said active agent.

19. The pharmaceutical composition of claim 18, wherein said absorption enhancer is a surface active agent.

20. The pharmaceutical composition of claim 19, wherein said surface active agent is absorbable or biodegradable.

21. The pharmaceutical composition of claim 19, wherein said surface active agent is selected from the group consisting of acylcarnitines, phospholipids and bile acids.

22. The pharmaceutical composition of claim 19, wherein said enhancer is an acyl carnitine.

23. The pharmaceutical composition of claim 22, further including a sucrose ester.

24. The pharmaceutical composition of claim 18, wherein said absorption enhancer is a surface active agent selected from the group consisting of (i) an anionic agent that is a cholesterol derivative, (ii) a mixture of a negative charge neutralizer and an anionic surface active agent, (iii) non-ionic surface active agents, and (iv) cationic surface active agents.

25. The pharmaceutical composition of claim 18, wherein said absorption enhancer is selected from the group consisting of a cationic surfactant and an anionic surfactant that is a cholesterol derivative.

26. The pharmaceutical composition of claim 18, wherein said pharmaceutical composition includes at least two absorption enhancers, one of which is a cationic surface active agent, and another of which is an anionic

surface active agent that is a cholesterol derivative.

27. The pharmaceutical composition of claim 26, wherein said anionic surface active agent is an acid-soluble bile acid.

28. The pharmaceutical composition of claim 3, further comprising an amount of a peptide that is not a physiologically active peptide effective to enhance bioavailability of said parathyroid hormone analog.

29. The pharmaceutical composition of claim 7, further comprising a water soluble barrier that separates said pH-lowering agent from said protective vehicle.

30. The pharmaceutical composition of claim 7, wherein said composition includes at least one pH-lowering agent that has a pKa no higher than 4.2.

31. The pharmaceutical composition of claim 7, wherein at least one pH-lowering agent has a solubility in water of at least 30 grams per 100 milliliters of water at room temperature.

32. The pharmaceutical composition of claim 8, wherein all ingredients other than said protective vehicle are uniformly dispersed.

33. The pharmaceutical composition of claim 32, wherein said pharmaceutical composition comprises granules containing a pharmaceutical binder and, uniformly dispersed in said binder, said pH-lowering

agent, said absorption enhancer and said peptide active agent.

34. The pharmaceutical composition of claim 18, wherein said composition is a solid dosage form wherein a weight ratio of said pH-lowering agent to said absorption enhancer is between 3:1 and 20:1.

35. The pharmaceutical composition of claim 18, wherein said composition is a solid dosage form wherein the weight ratio of said pH-lowering agent to said absorption enhancer is between 5:1 and 10:1.

36. The pharmaceutical composition of claim 7, wherein said pH-lowering agent is selected from the group consisting of citric acid, tartaric acid and an acid salt of an amino acid.

37. The pharmaceutical composition of claim 7, wherein said pH-lowering agent is present in an amount not less than 300 milligrams.

38. The pharmaceutical composition of claim 37, wherein said pH-lowering agent is present in an amount which is not less than 400 milligrams.

39. The pharmaceutical composition of claim 8, wherein said protective vehicle is a viscous protective syrup.

40. The pharmaceutical composition of claim 36, wherein a water soluble barrier separates said pH-

lowering agent from said protective vehicle.

41. A method for preventing or treating osteoporosis comprising administering to a subject in need thereof a pharmaceutically effective amount of a C-terminal amidated human parathyroid hormone analog selected from the group of a C-terminal amidated SEQ ID No 20 and a C-terminal amidated SEQ ID No 21.

42. The method of claim 41, wherein said administration is oral.

43. The method of claim 42, wherein said C-terminal amidated human parathyroid hormone analog is selectively released together with at least one agent selected from the group of a pH-lowering agent, a protease inhibitor, and a combination thereof into a patient's intestine following passage of said analog, pH-lowering agent and/or protease inhibitor through said patient's mouth and stomach under protection of an acid resistant protective vehicle which substantially prevents contact between stomach proteases and said analog.

44. The method of claim 43, wherein the release of said peptide active agent into a patient's intestine is carried out in the presence of at least one absorption enhancer effective to promote bioavailability of said peptide active agent.

45. A method for accelerating the healing of a broken bone comprising administering to a subject in need thereof a pharmaceutically effective amount of a C-

terminal amidated human parathyroid hormone analog selected from the group of a C-terminal amidated SEQ ID No 20 and a C-terminal amidated SEQ ID No 21.

46. The method of claim 45, wherein said administration is oral.

47. The method of claim 46, wherein said C-terminal amidated human parathyroid hormone analog is selectively released into a patient's intestine together with at least one agent selected from the group of a pH-lowering agent, a protease inhibitor, and a combination of the foregoing following passage of all orally administered ingredients through said patient's mouth and stomach under protection of an acid resistant protective vehicle which substantially prevents contact between stomach proteases and said analog.

48. The method of claim 47, wherein the release of said peptide active agent into a patient's intestine is carried out in the presence of at least one absorption enhancer effective to promote bioavailability of said peptide active agent.

49. A pharmaceutical composition for oral delivery of a physiologically active peptide agent selected from the group of a C-terminal amidated SEQ ID No 20 and a C-terminal amidated SEQ ID No 21 comprising:

(a) a therapeutically effective amount of said active peptide;

(b) at least one pharmaceutically acceptable pH-lowering agent;

(c) at least one absorption enhancer effective to promote bioavailability of said active agent; and

(d) an acid resistant protective vehicle effective to transport said pharmaceutical composition through the stomach of a patient while preventing contact between said active peptide active agent and stomach proteases;

wherein said pH-lowering agent is present in said pharmaceutical composition in a quantity which, if said composition were added to ten milliliters of 0.1M aqueous sodium bicarbonate solution, would be sufficient to lower the pH of said solution to no higher than 5.5.

50. A pharmaceutical composition for oral delivery of a physiologically active peptide agent selected from the group of a C-terminal amidated SEQ ID No 20 and a C-terminal amidated SEQ ID No 21 comprising a therapeutically effective amount of said active peptide linked to a membrane translocator, said membrane translocator is capable of being at least partially cleaved from the active peptide in vivo by an enzyme.